Sequential Treatment with Calcium Alginate Dressings and Hydrocolloid Dressings Accelerates Pressure Ulcer Healing in Older Subjects: A Multicenter Randomized Trial of Sequential versus Nonsequential Treatment with Hydrocolloid Dressings Alone

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OBJECTIVES: To compare the efficacy of a sequential strategy combining calcium alginate and hydrocolloid dressings treatment of grade III or IV pressure ulcers (PUs) and the efficacy of nonsequential strategy with hydrocolloids alone.

DESIGN: An open, randomized, multicenter parallel-group trial.

SETTING: Twenty geriatrics hospital wards.

PARTICIPANTS: One hundred ten older patients with grade III or IV PUs.

INTERVENTION: The control strategy consisted of applying hydrocolloid dressings (DuodermE) for 8 weeks; the sequential strategy consisted of applying combined calcium alginate dressings (UrgoSorb) for the first 4 weeks and hydrocolloid dressings (Algoplaque) for the next 4 weeks.

MEASUREMENTS: PU surface areas were measured weekly by ulcer tracing. The endpoints were the mean absolute surface area reduction (SAR) during the 8-week study period and the number of patients achieving a 40% or more SAR (SAR_{40}).

RESULTS: Fifty-seven and 53 patients were randomly allocated to sequential and control strategies respectively. Baseline patient characteristics and PU ulcer features at inclusion were similar in the two groups. Mean ± standard deviation SAR was significantly larger in the sequential treatment group (5.4 ± 5.7 cm^2 and 7.6 ± 7.1 cm^2 at 4 and 8 weeks) than in the control group (1.6 ± 4.9 cm^2 and 3.1 ± 7.2 cm^2, $P < .001$). In the sequential treatment group, 68.4% of the patients reached SAR_{40} at 4 weeks and 75.4% at 8 weeks, proportions significantly larger than in the control group (22.6% and 58.5%, respectively, $P < .0001$). Dressing tolerance was good in both strategies.

CONCLUSIONS: In grade III or IV PUs, treatment using first calcium alginate dressings and then hydrocolloid dressings promotes faster healing than treatment with hydrocolloid dressings alone. **J Am Geriatr Soc 50:269–274, 2002.**

Key words: calcium alginate dressing; hydrocolloid dressing; pressure sores; older people; randomized controlled trial

Pressure ulcers (PUs) are a common problem in older subjects admitted to hospitals or living in nursing homes.[1–3] They are responsible for high morbidity and impaired quality of life and require time-consuming and costly treatments that delay hospital discharge.[4–6]

Local treatment of PUs is based on careful nursing and use of dressings, to protect the wound and create an environment favorable to healing. During the last decades, considerable advances have been made in understanding the healing process,[7–9] leading to the design of new types of dressings. An increasing number of wound dressings are available, but there are few controlled studies for the comparison of different types of dressings. Most of the existing studies have documented the efficacy of hydrocolloid dressings in the management of chronic wounds.[10–13] In PUs, hydrocolloid dressings have been compared with wet-to-dry dressings[14] and with saline gauze dressings[15–17] and now appear to be one of the reference treatments of PUs.[18–21]

Wound debridement is the first step in the course of treatment of an established PU. This process is important, because tissue granulation cannot occur until necrotic material and debris are removed. However, it can take a long time to debride a PU completely, especially in frail older patients

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DuodermE® is the same product as DuodermCGF® in the United States, GranuflexE® in the United Kingdom, and Varihesive® in Germany. Algoplaque® is the same product as Sorbex® in the United States.

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who frequently cannot undergo surgical debridement. Because calcium alginate dressings have been shown to help the debridement of PUs,[22–24] we wondered whether a sequential strategy using first calcium alginate and then hydrocolloid dressings would lead to faster PU healing in older patients, than nonsequential treatment with hydrocolloid dressings alone.

METHODS

This 8-week, open-label, randomized, parallel group study was conducted in 20 French geriatric hospital wards. Patients aged 65 and older were considered for participation if they suffered from PUs that passed through the subcutaneous tissue (grades III and IV of Yarkony's classification[25]). In patients with several grade III or IV PUs, only one ulcer was selected for study. Patients were eligible if the target ulcer met four criteria: location on the sacrum, elsewhere on the pelvic girdle, or on the heel; surface area of less than 50 cm^2, as measured by planimetry; granulation tissue area not covering more than 50% of the ulcer surface, as visually estimated by the investigator; and no clinical evidence of active local infection. Patients were not eligible if their serum albumin concentration was below 25 g/L; if they were being treated with radiotherapy, cytotoxic drugs, or corticosteroids; or if surgical or palliative care was needed. Written consent was obtained from each subject before inclusion. Baseline parameters were age, sex, height, body weight, medical and surgical history, and Norton score,[26,27] which documents risk factors for PUs based on mobility status, neurological and mental condition, and incontinence. For each participant, we recorded previous history of PUs and the location, grade, duration, and appearance of the surrounding skin of the target ulcer. Blood was sampled for serum albumin determination.

The Ethics Committee of Versailles (France) approved the study protocol, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Treatment of Pressure Ulcers

Each patient was randomized to one of the two treatment strategies. The randomization was balanced by center and by blocks of four patients. The control strategy consisted of applying hydrocolloid dressings (DuodermE®, Convatec-Bristol Myers Squibb, France) for 8 weeks. The sequential strategy consisted of applying calcium alginate dressings (UrgoSorb®, Urgo, France) for the first 4 weeks, and then hydrocolloid dressings (Algoplaque®HP, Urgo, France) for the next 4 weeks. The UrgoSorb dressing is a nonwoven dressing composed of calcium alginate fibers and carboxymethylcellulose; alginates were obtained from brown seaweeds. Both the Algoplaque and DuodermE dressings comprise an outer layer of polyurethane and an inner layer formed by an elastomere matrix that includes hydrocolloid molecules (carboxymethylcellulose, pectin, and gelatin). In patients with deep PUs, investigators were allowed to prescribe a hydrocolloid paste while hydrocolloid dressings were being applied (DuodermE Pâte in the control group and Algoplaque Pâte in the sequential treatment group). However, for the patients in the sequential treatment group with deep PUs, no paste was added to the calcium alginate dressing. No other debridement therapy such as enzymes, hydrotherapy, or surgical debridement was used during the trial.

Because the appearance and use of the hydrocolloid and alginate dressings were very different, it was not possible to conduct the trial under blinded conditions. Before it started, the nursing staff of all the participating centers were trained in the use, supervision, and removal of the dressings. During the trial, nurses examined dressings daily and changed them if necessary according to a protocol standardized for the study. Hydrocolloid dressings were removed every third day or more often if the area discolored by exudate was less than 1 cm from the edge of the dressing or if a leakage was apparent. Calcium alginate dressings were removed every other day or more often if they were saturated, especially when exudate appeared through the secondary dressing.

Other aspects of local care were standardized for all patients. In particular, ulcers were cleansed with sterile saline, and the surrounding skin was dried before applying dressings. For all patients, general treatment (nutrition, medication, and the use of mattress and cushion) was decided by each investigator according to their usual procedure of care and to the patient's health status.

Endpoints and Ulcer Healing Assessment

The main endpoints were the evolution of the surface area reduction (SAR) during the trial and the percentage of patients whose ulcer reached a 40% or more SAR (SAR_{40}). SAR was calculated for each week of the trial as an absolute value and a percentage ((100 × (baseline surface area minus actual surface area))/baseline surface area). The secondary endpoint was dressing tolerance.

Ulcer surface area was measured by planimetry at inclusion and then weekly during the trial. After cleansing and drying, a sterile transparent polyurethane film was applied to the target ulcer, and the investigator traced its perimeter with a permanent ultra-fine-tipped marker. A photograph of the ulcer was also taken (Canon EOS 1000 camera, Tokyo, Japan). Area tracings and photographs were performed according to the same standardized protocols in all centers. For each tracing, the surface area was measured in triplicate by an independent investigator unaware of treatment allocation, using a digitalization table and computer program (AutoCAD), and the mean value was included in the analysis.

When dressings were removed, nurses recorded information about the general features of the ulcer and pain during care, to detect any adverse event before the next medical visit. For each act of care, they assessed the ease of dressing removal on a 2-item scale (easy/very easy, difficult), the presence or absence of pain during dressing removal, and the presence of odor on a 3-item scale (none, mild, strong).

Statistics

The size of the study was designed to allow detection of a 35% difference between groups in the number of patients reaching SAR_{40}, with a 5% alpha risk and an 80% study power. Statistical analysis was conducted on the intention-to-treat population using SAS software. Comparisons between groups were performed using chi-square test for qualitative parameters and the Mann-Whitney *U* test for

quantitative variables. The percentage of patients reaching SAR_{40} was analyzed by the Kaplan-Meier method, and treatment groups were compared using the logrank test. The evolution of SAR during the trial was analyzed by repeated-measurement analysis of variance, to investigate the effect of time and treatment. Tests were bilateral, and the significance threshold was fixed at .05.

RESULTS

Patients

Of the 110 patients included (71% women, mean age ± standard deviation (SD) = 83.5 ± 7.6), 57 were randomized to the sequential strategy and 53 to the control strategy. The baseline characteristics of the two groups were similar (Table 1), except for hypertension and diabetes mellitus, which were more frequent in the sequential treatment group. No significant differences between groups were found in the baseline characteristics of the target PU (Table 2). Most PUs were grade III (75.5%) and were predominantly located on the heel and sacrum. The mean surface area of ulcers at baseline was 14.7 ± 10.4 cm^2 in the sequential group and 12.6 ± 8.0 cm^2 in the control group (NS). The 25%, 50%, and 75% percentiles for ulcer area were, respectively 7.4 cm^2, 11.3 cm^2, and 14.4 cm^2 in the sequential treatment group; the corresponding values in the control group were 6.4 cm^2, 10.1 cm^2, and 17.8 cm^2. In most cases, they had been covered with a hydrocolloid dressing before randomization (Table 2). In four patients in the sequential treatment group and three in the control group, the ulcer was located on the lateral border of the foot. In another patient, the ulcer's surface area (56.7 cm^2) was slightly above the limit set by the inclusion criteria. However, these features were considered to be minor deviations from the protocol, and the patients were included in the analysis. In all, the PUs of 11 patients (10.0%, 95% confidence interval = 5.1–17.2%) healed completely in the course of the study (three in the sequential treatment group and eight in the control group; $P = .162$).

Thirty-three patients of 110 (30%) did not complete the planned 8-week follow-up for reasons other than ulcer healing (Table 3); 11 patients in the sequential treatment group (19.3%) and eight in the control group (15.1%, NS) died during the study.

Surface Area Reduction

The PU surface areas measured during the trial are shown in Table 4. In the sequential treatment group, 39 (68.4%) patients reached SAR_{40} at 4 weeks and 43 (75.4%) (cumulative) at 8 weeks; in the control group, 12 (22.6%) and 31 (58.5%) patients reached SAR_{40} at 4 and 8 weeks, respectively. The difference in SAR_{40} between groups was highly significant during the trial ($P < .0001$, logrank test; Figure 1). Compared with the baseline value, PU surface area was reduced by 7.0 ± 5.7 cm^2 at 4 weeks and by 9.7 ± 7.1 cm^2 at 8 weeks in the sequential treatment group, and by 1.6 ± 4.9 cm^2 and 5.2 ± 7.2 cm^2, respectively, in the control group ($P < .001$). Expressed as a percentage, SAR at 4 weeks diminished by 47.3 ± 30.0% in the sequential group and by 14.6 ± 39.7% in the control group ($P < .001$). At 8 weeks, the corresponding values were 69.1 ± 33.9% and 42.6 ± 49.1%, respectively ($P < .001$, Figure 2). Moreover, we verified that excluding the patient with the ulcer area exceeding 50 cm^2 from analysis did not alter the conclusions of the statistical analysis on SAR.

Tolerance Assessed by Nurses

During the trial, 1,314 dressings (804 calcium alginate and 497 hydrocolloid) were used in the sequential treatment group and 879 in the control group. The mean number of

Table 1. Baseline Characteristics of Older Patients with Pressure Ulcers Treated Sequentially with Alginate + Hydrocolloid Dressings or Hydrocolloid Dressings Alone (Control)

Characteristic	Sequential Treatment Group (n = 57)	Control Group (n = 53)	*P*-Value
Women, n (%)	42 (74)	36 (68)	.506
Age, years, mean ± SD	84.8 ± 7.1	82.2 ± 7.9	.078
Body weight, kg, mean ± SD	56.9 ± 10.2	56.9 ± 13.6	.994
Height, cm, mean ± SD	162.6 ± 7.2	160.7 ± 10.1	.290
Serum albumin, g/l, mean ± SD	29.3 ± 4.0	29.5 ± 3.9	.981
Risk factors for pressure ulcers			
Norton score, mean ± SD	13.2 ± 3.4	12.6 ± 3.1	.336
Totally bedridden, n (%)	8 (14)	10 (19)	
Poor health status, n (%)	14 (25)	14 (26)	
Comatose or apathetic, n (%)	38 (67)	38 (72)	
Urinary and fecal incontinence, n (%)	27 (47)	26 (49)	
Concomitant diseases			
Diabetes mellitus, n (%)	17 (29.8)	7 (13.2)	.035
Hypertension, n (%)	29 (51.0)	17 (32.1)	.046
Heart disease, n (%)	22 (39.1)	25 (48.1)	.357
Neurologic/psychiatric disease, n (%)	36 (63.2)	36 (67.9)	.599
Peripheral arterial disease, n (%)	16 (28.1)	12 (23.1)	.551

SD = standard deviation.

Table 2. Baseline Characteristics of Pressure Ulcers

Characteristic	Sequential Treatment Group (n = 57)	Control Group (n = 53)	*P*-Value
Ulcer grade			.166
III, n (%)	40 (71.4)	43 (82.7)	
IV, n (%)	16 (28.6)	9 (17.3)	
Ulcer location			.621
Sacrum, n (%)	14 (24.6)	11 (20.8)	
Pelvic girdle, n (%)	5 (8.8)	2 (3.8)	
Heel, n (%)	34 (59.6)	37 (69.8)	
Other, n (%)	4 (7.0)	3 (5.7)	
Duration, weeks, mean ± SD	7.2 ± 6.8	7.7 ± 6.6	.686
Surface area, cm², mean ± SD	14.7 ± 10.4	12.6 ± 8.0	.245
Range			
Previous dressings	4.1–57.2	3.6–37.8	.325
Hydrocolloid, n (%)	30 (52.6)	27 (50.9)	
Calcium alginate, n (%)	8 (14.0)	3 (5.7)	
Saline gauze, n (%)	6 (10.5)	8 (15.1)	
Enzymes, n (%)	8 (14.0)	7 (13.2)	
Others, n (%)	5 (8.8)	8 (15.1)	

SD = standard deviation.

dressings per week was significantly greater in the sequential treatment group. The nurses in the two groups scored ease of removal similarly. Pain during dressing removal and odor were significantly less in the sequential treatment group (Table 5).

Adverse Events

Reasons for dropping out of the trial are shown in Table 3. Adverse events were reported for 11 patients (six in the sequential treatment group and five in the control group, NS). All the local adverse events recorded in the control group were due to excessive granulation.

Table 3. Reasons for Dropping Out and Local Adverse Events During the Trial

Variable	Sequential Treatment Group (n = 57)	Control Group (n = 53)
	n	
Reasons for dropping out		
Death	11	8
Transfer to another care unit	1	2
Worsening health status	1	0
Local adverse event	1	3
Pressure ulcer impairment	3	3
Adverse local events		
Infection	1	0
Erythema of the surrounding skin	2	0
Hypergranulation	1	5
Maceration	1	0
Bleeding	1	0

Table 4. Evolution of Ulcer Surface Areas Over Time

Week	Surface Area (cm²)	
	Sequential Treatment Group (n = 57)	Control Group (n = 53)
	mean ± SD	
0	14.7 ± 10.4	12.6 ± 8.0
1	10.9 ± 7.3	12.4 ± 8.7
2	9.7 ± 7.4	12.4 ± 9.4
3	8.8 ± 7.6	11.6 ± 8.6
4	7.7 ± 7.6	11.0 ± 9.4
5	7.0 ± 8.6	9.5 ± 9.9
6	6.2 ± 8.1	8.4 ± 10.2
7	5.8 ± 8.0	7.7 ± 9.2
8	5.0 ± 8.2	7.4 ± 10.2

Note: $P < .001$ for differences between groups (analysis of variance).
SD = standard deviation.

DISCUSSION

This randomized trial shows that, in older patients, a sequential therapeutic strategy consisting of calcium alginate dressings followed by hydrocolloid dressings clearly led to faster healing of full-thickness PUs in the debridement phase than standard nonsequential treatment with hydrocolloid dressings alone. This finding might have important clinical implications for treating older patients with Yarkony grade III or IV PUs and might help to improve their outcome and shorten their hospital stay.

Assessing the efficacy of dressings for wound healing is a complex problem, for specific methodological reasons. Standard drug trial methods cannot be directly applied to

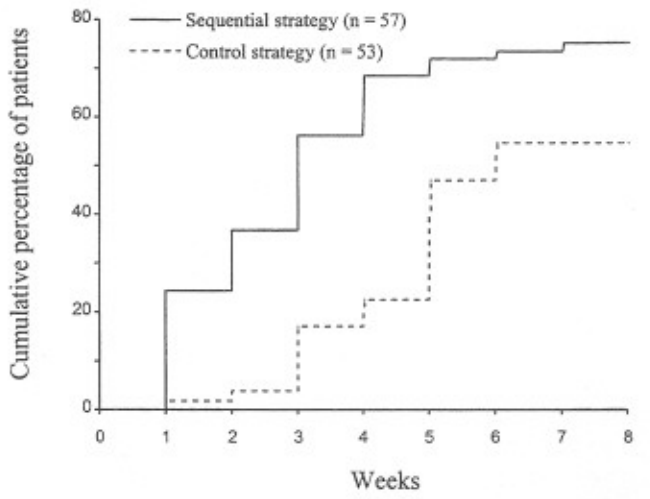

Figure 1. Cumulative percentage of patients reaching a 40% pressure ulcer surface area reduction over 8 weeks in the groups undergoing sequential treatment (n = 57) and control treatment (n = 53).

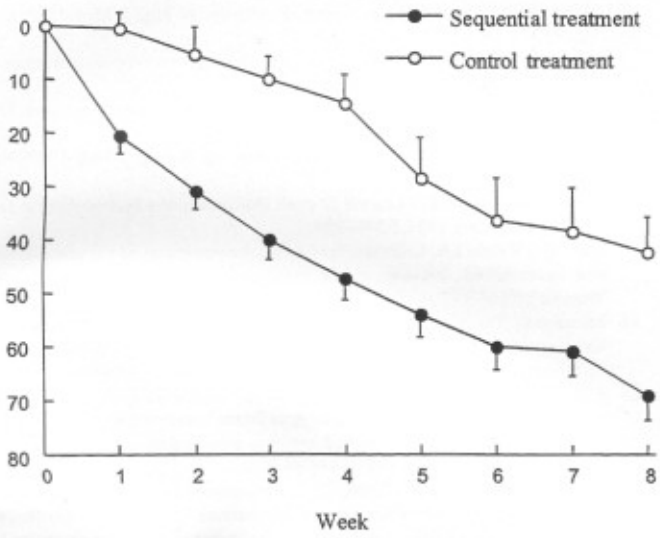

Figure 2. Pressure ulcer surface area reduction (mean ± standard error of the mean) during the trial expressed as percentage of change from baseline. The difference between groups is significant ($P < .001$).

such assessment. The use of a "placebo dressing" is not possible, and comparison of two or more different dressings is required. Moreover, it is quite impossible to give the dressings to be compared a similar appearance, and, therefore, clinical trials cannot be double-blinded. In this study, we attempted to overcome this problem by ensuring that the technical investigator who computed and measured ulcer areas was independent of the clinical investigators and was blinded to the treatment allocated. Nevertheless, despite the methodological difficulties involved in such trials, it seems important to conduct them so as to compare the efficacy of dressings and thus help physicians prescribe the most appropriate therapy for patients with PUs.

Because wound healing is a dynamic and highly complex process,[9] a strategy using different dressings for different PU phases (e.g., alginate for debridement and hydrocolloids for tissue granulation) might be better than standard treatment using hydrocolloid dressings for all PU phases. The results of the present study support our hypothesis that the use of alginate dressings during the debridement phase accelerates the healing of PUs. However, it should be noticed that we used different brands of hydrocolloid dressing in the two treatment strategies. This, rather than the use of alginate in the sequential strategy, might be responsible for the differences in their outcomes. However, we believe this is unlikely, because the differences between healing rates were striking during the first 4 weeks of the trial and because SAR was diminished by 47% with the sequential strategy but only by 15% with the control strategy. By contrast, during the last 4 weeks of the trial, healing rates were similar in the two groups, because SAR further diminished by 35% and 33% in the sequential and control groups, respectively. In addition, because of their occlusiveness and to the mixture of wound fluid and hydrocolloid molecules they contain, hydrocolloid dressings are known to promote healing by keeping the ulcer moist. Therefore, the two types of hydrocolloid dressing used in the trial had the same mechanisms of action, and it is unlikely that their effects on the healing rate were very different.

As far as we know, this is the first investigation study in which the efficacy of a sequential local treatment of PUs was evaluated. The sequential approach we chose was based of the biological properties of the dressings. Alginates are gel-forming dressings that absorb wound exudate to form a nonadherent gel that maintains a moist environment.[28] In addition, when encapsulated by alginates, murine or human macrophages were found to be activated and to secrete cytokines.[29–31] These effects might help to clear necrotic debris and stimulate angiogenesis, which in turn might help ulcer debridement. However, other in vitro experiments showed that calcium alginates stimulate fibroblast proliferation and reduce the proliferation of human microvascular endothelial cells and keratinocytes.[32] Consequently, as soon as the granulation tissue is well developed, the maintenance of an alginate dressing may promote excessive granulation, which might delay re-epithelialization. It is therefore necessary to switch to the use of a more neutral dressing, such as a hydrocolloid dressing, which maintains a moist environment but is not known to activate macrophages.

In the present study, we chose a 4-week period for alginate application, on the basis of a previous randomized trial comparing the healing effect of alginate dressing and dextranomer paste on PUs.[22] In that study, the median time required for SAR_{40} was 4 weeks in the alginate dressing group. Nevertheless, a more optimized approach to the decision to switch from alginate to another dressing might be individualized by considering the feature of each patient's ulcer. A clear SAR_{40} combined with active granulation might constitute a reason for changing the type of dressing. However, such an approach was considered to be difficult to implement in the framework of a multicenter trial and therefore a more pragmatic method with fixed periods of time was chosen here and was found to be satisfactory.

The question of whether the shorter healing process observed in the sequential treatment group might translate into a shorter time required for complete healing is not an-

Table 5. Aspects of Ulcer Care Recorded by Nurses for all Changes of Dressing During the 8-Week Trial

Aspect of Care	Sequential Treatment Group (n = 1,314)	Control Group (n = 887)	*P*-Value
Number of dressings removed per week, mean ± SD	3.8 ± 1.6	2.9 ± 1.0	.01
Ease of removal			.11
Difficult, %	7.6	9.6	
Easy or very easy, %	92.4	90.4	
Pain during removal			.03
Yes, %	31.3	35.6	
No, %	68.7	64.4	
Odor			.001
Strong, %	13.2	20.1	
Mild, %	29.1	40.7	
None, %	57.8	39.1	

SD = standard deviation.

swered in our study and was not the objective of this trial. To answer it would have required a much longer follow-up period and a considerably larger sample population. Furthermore, conducting longer trials in such frail older patients is difficult, because of high dropout rates and the high incidence of intercurrent disease, which lead to changes in the general care of the patients. The initial healing rate was found be a good predictor of complete healing in leg ulcers,[33] but this has not been documented in PUs. However, even if the present healing rate is an intermediate outcome, we believe it can be considered clinically relevant.

In conclusion, the PU healing process is accelerated by a more physiological approach consisting of local sequential treatment. The first step in this treatment is to stimulate debridement and macrophage activation. Then, once granulation is well developed, the second step is simply the maintenance of a moist environment.

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REFERENCES

1. Allman RM. Pressure ulcer prevalence, incidence, risk factors, and impact. Clin Geriatr Med 1997;13:421–436.
2. Berlowitz DR, Anderson JJ, Brandeis GH et al. Pressure ulcer development in the VA: Characteristics of nursing homes providing best care. Am J Med Qual 1999;14:39–44.
3. Thoroddsen A. Pressure sore prevalence: A national survey. J Clin Nurs 1999;8:170–179.
4. Berlowitz DR, Brandeis GH, Anderson J et al. Effect of pressure ulcers on the survival of long-term care residents. J Gerontol A Biol Sci Med Sci 1997;52A: M106–M110.
5. Perneger TV, Heliot C, Rae AC et al. Hospital-acquired pressure ulcers: Risk factors and use of preventive devices. Arch Intern Med 1998;158:1940–1945.
6. Allman RM. Pressure ulcers among the elderly. N Engl J Med 1989;320: 850–853.
7. Hinmann CC. Effect of air exposure and occlusion on experimental human skin wound. Nature 1963;200:377–379.
8. Winter G.D. Effect of air drying and dressings on the surface of wounds. Nature 1963;197:91–93.
9. Singer AJ, Clark RA. Cutaneous wound healing. N Engl J Med 1999;341: 738–746.
10. Schmitt M, Vergnes P, Canarelli JP et al. Evaluation of a hydrocolloid dressing. J Wound Care 1996;5:396–399.
11. Scurr JH, Wilson LA, Coleridge Smith PD. A comparison of calcium alginate and hydrocolloid dressings in the management of chronic venous ulcers. Wounds 1994;6:1–7.
12. Hansson C. The effects of cadexomer iodine paste in the treatment of venous leg ulcers compared with hydrocolloid dressing and paraffin gauze dressing. Cadexomer Iodine Study Group. Int J Dermatol 1998;37:390–396.
13. Agren MS, Everland H. Two hydrocolloid dressings evaluated in experimental full-thickness wounds in the skin. Acta Derm Venereol 1997;77:127–131.
14. Gorse GJ, Messner RL. Improved pressure sore healing with hydrocolloid dressings. Arch Dermatol 1987;123:766–771.
15. Colwell JC, Foreman MD, Trotter JP. A comparison of efficacy and cost-effectiveness of two methods of managing pressure ulcers. Decubitus 1993;6:28–36.
16. Xakellis GC, Chrischilles EA. Hydrocolloid versus saline-gauze dressings in treating pressure ulcers: A cost-effectiveness analysis. Arch Phys Med Rehabil 1992;73:463–489.
17. Alm A, Hornmark AM, Fall PA et al. Care of pressure sores: A controlled study of the use of hydrocolloid dressings compared with wet saline gauze compresses. Acta Derm Venereol 1989;149:1–10.
18. Day A, Dombranski S, Farkas C et al. Managing sacral pressure ulcers with hydrocolloid dressings: Results of a controlled, clinical study. Ostomy Wound Manage 1995;41:52–58.
19. Bale S, Squires D, Varnon T, Walker et al. A comparison of two dressings in pressure sore management. J Wound Care 1997;6:463–466.
20. Seeley J, Jensen J, Hutcherson J. A randomised clinical study comparing a hydrocellular dressing to a hydrocolloid dressing in the management of pressure ulcers. Ostomy/Wound Manage 1999;45:39–47.
21. Thomas S, Banks V, Bale S et al. A comparison of two dressings in the management of chronic wounds. J Wound Care 1997;6:383–386.
22. Sayag J, Meaume S, Bohbot S. Healing properties of calcium alginate dressings. J Wound Care 1996;5:357–362.
23. Barnett SE, Varley SJ. The effects of calcium alginate on wound healing. Ann R Coll Surg 1987;69:153–155.
24. Piaquidio D, Nelson DB. Alginates: A new dressing alternative. J Dermatol Surg Oncol 1992;18:992–995.
25. Yarkony GM, Kirk PM, Carlson C et al. Classification of pressure ulcers. Arch Dermatol 1990;126:1218–1219.
26. Norton D, Mac Laren L, Exton Smith AN. An Investigation of Geriatric Nursing Problems in Hospital. National Corporation for the Care of Old People. Edinburgh: Churchill Livingston, 1975.
27. Norton D. Calculating the risk: Reflections on the Norton Scale. Adv Wound Care 1996;9:38–43.
28. Ichioka S, Harii K, Nakahara M et al. An experimental comparison of hydrocolloid and alginate dressings, and the effect of calcium ions on the behaviour of alginate gel. Scand J Plast Reconstr Surg Hand Surg 1998;32:311–316.
29. Pueyo ME, Darquy S, Capron F et al. In vitro activation of human macrophages by alginate-polylysine microcapsules. J Biomater Sci Polym Ed 1993;5: 197–203.
30. Otterlei M, Ostgaard K, Skjak-Braek G et al. Induction of cytokine production from human monocytes stimulated with alginate. J Immunother 1991; 10:286–291.
31. Tahri Jouti MA, Ramdi H, Lievremont M. Effect of alginate de calcium on secretion of IL 1 by immobilized Swiss peritoneal macrophages. Biomater Artif Cells Immobilization Biotechnol 1993;21:353–358.
32. Doyle JW, Roth TP, Smith RM et al. Effects of calcium alginate on cellular wound healing processes modeled in vitro. J Biomed Mater Res 1996;32: 561–568.
33. Tallman P, Muscare E, Carson P et al. Initial rate of healing predicts complete healing of venous ulcers. Arch Dermatol 1997;133:1231–1234.